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Colorimetric detection based on gold nano particles (GNPs): An easy, fast, inexpensive, low-cost and short time method in detection of analytes (protein, DNA, and ion)

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ABSTRACT

Gold nanoparticles (GNPs), due to their unique physical and chemical properties, including optical properties, are highly regarded and have extensive applications in biomedical. One of the applications of gold nanoparticles is detection of chemical and biological material, so that these particles are used in detection of materials based on gold nanoparticles being in aggregate and non- aggregate modes and the change in the color of the nanoparticle solution as a result of this change of mode. In the interaction of gold nanoparticles (Bare nanoparticles or functionalized with different compositions) with analytes, aggregate and non-aggregate mode of nanoparticles changes and finally the change in the color of the solution is seen with naked eye without the need for advanced and costly equipment, indicating the presence or absence of target analytes. This change of mode and the subsequent color change is the basis of colorimetric detection based on gold nanoparticles in detection of various analytes. Various analytes can be detected by this method include ion, nucleic acid, proteins and peptides. In this study, we have reviewed various studies performed based on colorimetric detection using gold nanoparticles in detection of various analytes. According to these studies, simplicity, speed, time and cost savings are of considerable benefits of this method, compared to other detection methods.

1. Introduction

1.1. Gold nano particles (GNPs)

Nano biotechnology has expanded rapidly in recent years in various biological fields, in fact, nanoparticles, due to having unique physical and chemical characteristics such as chemical surface, size, shape-dependent electronic, and compatibility with surface functionalization, simple use and also optical properties [1–3], are highly regarded and are subject to research as well as application in biology and medicine. One of the common nanoparticles with unique properties and extensive application in biomedical are gold nanoparticles [3], that are an important substance in nanotechnology with various applications in biosensing.

The scope of the use of gold nanoparticles in biomedical is heavily expanded, its common applications include electrochemical biosensors [4], vaccine development [5], drug delivery [6], biosensorics, immunoassay and detection [2]. The basis of this wide range of uses of these particles is the unique chemical and physical properties of them. On the other hand, detection of chemical and biological material in biomedical and environmental is also of great importance and properties such as high sensitivity and specificity, cost-effective, convenience, time saving as well as low detection of limits (LOD) are very important and significant in chemical and biological material detection methods. Given the specific physical and chemical properties of nanoparticles, including gold nanoparticles, these particles can be used as biological and chemical sensors in detection methods of material and analytes [7].

2. Using GNPs in detection and diagnostic

2.1. SPIA

Sol-Particle Immunoassay (SPIA)Technique was proposed for the first time in 1980 by Leuvering et al. for detection of materials based on gold nanoparticles getting aggregation reaction with macromolecules such as proteins. Therefore, that examination of color change in

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solution both by uv-visible (vis) spectrophotometer and also visually and the solution color changes from red to blue/purple. Thus, the SPIA method based on the aggregation of gold nanoparticles conjugated with monoclonal antibodies was presented against of various antigens for detection [8]. Among the substances examined in this way in several studies is measuring human chorionic gonadotrophin hormone (HCG) that is performed using conjugated gold nanoparticles anti-HCG. In measurement of HCG by the SPIA method in urine, the gold nanoparticles (40 nm) conjugated anti-HCG was used in order to agglutination of HCG-anti-HCG, indicates a change in spectrum absorbance of nanoparticles. Also at high concentrations of HCG color changes from red to blue is done faster which indicates this technique is basically a colorimeter [9]. Other studies in 1980 and 1983 have also examined and detected HCG hormone with this method [10–13].

Other analytes that have been previously subjected to this detection method are anti-rubella antibody [14], level determination of Selenoprotein P (SeP) of serum that maintains selenium in the tissue [15]. Serum cyctatin C (cyc C) which is marker of glomerular filtration rate (GFR) [16,17], detection of the trypsin enzyme (the pancreatic serine protease, which digest the protein in the intestines) and IgG with a 15 nm conjugated nanoparticle with protein A, that protein A attaches to an Fc antibody with high affinity [8], detection of all isotypes of IgG [18]. And also, estrogen in urine and serum [19] and identification of Calprotectin in serum of IBD disease [20]. In the last case (identification of Calprotectin), the results of this method have been compared with the results of the ELISA method. It has been observed that the performance and efficacy of this procedure are similar to that of ELISA, but because of its simplicity, low cost, time saving and high speed compared to ELISA, this technique can be more appropriate for clinical use [20].

2.2. Using GNPs in colorimetric detection

The gold nanoparticle solution (15 nm) is red-ruby, which has a maximum absorption length in this mode as (disperse mode) at 520 nm. With the aggregation of the gold nanoparticles, its size is changed, the color of the solution changes to blue/purple, and the absorption peak will be higher in high wavelengths [21]. The gold nanoparticle aggregation is mainly associated with binding of surface ligands to target analytes, and when the target analytes are attached to a large number of AuNPs through ligand, the result is as aggregation of the nanoparticles and, finally, the change in the color of solution [22]. These surface ligands are the charged groups of nanoparticles surface or functional groups attached to nanoparticles that provides conditions for aggregation of nanoparticles in the interconnection with target analyzes. In Tables 1 and 2, functional groups conjugate to nanoparticles in different analyzes that are used in different studies are stated.

Changing the color of GNPs in different size is the most advantage of these particles based on colorimetric detection can be use in recognition of various analytes, such as DNA, protein and ion. This process is a two way approach so that during aggregation, we observe the change in color from red to blue/purple and in redispesion (separation), there is a change from blue/purple to red [23]. In fact, the change in SRP peak absorption is between the dispersed and aggregation modes of gold nanoparticles, which is observed as color changes [24].

Aggregation mechanisms; two different mechanisms of gold nanoparticles aggregation are: 1. Aggregation with cross-linking mechanism based on presence of molecules cross-linking, which creates the binding area of nanoparticles to target molecules, 2. There is no need for cross-linking molecules, in which target biomolecules themselves such as DNA and peptide act as Coagulant or Stabilizer of gold nanoparticles [25]. Various types of analytes including cells, proteins, DNAs, metal ions and small molecules can be detected using this method [22]. Colorimetric detection based on gold nanoparticles by creating detection conditions with naked eyes, its simplicity, speed and suitability for time-real and on-site detection, without the need for complex and expensive devices, and low amenability, as well as easy preparation of these nanoparticles, this method is superior to many other detection methods [22,23,26].

Colorimetry is a solution-based assay method that by measuring the absorption wavelength, can estimate the concentration of the material in the solution, and according to the specific properties of the gold nanoparticles, based on these particles colorimetry can be a suitable candidate for detection in these particles [3].

In general, the important feature of color change in gold nanoparticles in different aggregated and non-aggregated modes, followed by the detection colorimetric method which is a quick and simple method, and detection of various analytes just by observing color change with the naked eye cause effectiveness and simplicity of this method economically and timely in detecting analytes [21].

2.2.1. Detection of ions

Nowadays Chemical pollution in the environment is one of the most problems of the world. Thus, rapid and accurate detection of pollutants like toxic materials, organic and inorganic pollution, as well as heavy metal ions in environmental samples, including weather and water is one of the most important issues in environmental monitoring. Since given effects of these materials on the ecosystem and the consequent serious effects on health of individuals, the identification and elimination of these harmful substances from the environment, especially drinking water, is very valuable [27]. Due to this reason and unique properties of gold nanoparticles, such as optical properties (e.g., SPRs; surface Plasmon resonances), the use of these particles based on the method of colorimetric detection in the detection of ions, especially heavy metal ions in environmental samples such as drinking water and food and dairy products have been particularly studied in various studies. The ions that have been detected with this method and analyzed by Uv–vis spectroscopy and observed with naked eyes is Pb^{2+} ion, a water contamination with high toxicity [28], Hg^{2+} ion (Mercury (II): A heavy metal ion that has a high toxicity and detrimental effects on human health. This ion affects the function of the brain, heart, kidneys, stomach and intestines) [29], Ag^{+} ion which is one of the most dangerous ion contaminations in air, water and food [30], Cu^{2+} ion which is an essential ion in the human body and part of the enzymatic systems. But at higher concentrations has devastating effects and leads to oxidative stress and disorders related to neurodegenerative diseases [31], Nitrite ion (NO_2^-), which is part of the nitrogen cycle. This ion is harmful to humans and contains type A chemicals inorganic in water and needs to be monitored because it is highly toxic [32], detection of Ba^{2+} ion in environmental samples and industrial materials [33]. And also, Ca^{2+} ion in serum samples that this is the most important cation of the body that is involved in various biological activities such as neurotransmitter and instigating skeletal and cardiac muscles. Quick and accurate study of calcium levels is very important due to the fact that severe fluctuations occur in level of this ion occur in many diseases [34,35].

Detected ions by this method and with details such as the type of functional group associated with gold nanoparticles and detection of limit (LOD) listed in Table 1. As can be seen in this table, in addition to heavy metal ions, other ions, such as serum calcium ions, and uranyl (Uo_2^{2+}) ion that is a radioactive ion, have been examined and reported using 13 nm nanoparticles with detection limit 50 nM in water sample [36]. In these studies mainly stated that this method of ion detection is easy, fast, and efficient and without the need for complex equipment with the appropriate detection limit for ion detection.

2.2.2. Detection of nucleic acid

The DNA Colorimetric detection of nucleic acid using metallic nanoparticles, including DNA (DNA-functionalized GNPs), functionalized gold nanoparticles were first introduced by Mirkin and his colleagues using a DNA probe that in the presence of complementary probe DNA in soluble, the gold nanoparticles are aggregated [57]. On the other hand,

Table 1
Ions detected by the colorimetric detection method and detect details.

Ions	Size of nanoparticles	Detection of limit (LOD)	Gold nanoparticles	Detection method	Samples	Ref
Pb^{2+}	17 ± 2 & 36 ± 2 nm	53 Nm	L-Tyrosin stabilized AuNPs	Uv-visspectrometry & naked eye	Aqueous medium	[37]
	–	2 orders of magnitude higher than the EPA standard limit	GSH (Glutathione)-conjugated GNPs	Uv-visspectrometry & naked eye	Aqueous medium	[28]
	5-8 nm	100 nM	GSH-functionalized GNPs	Uv-visspectrometry & naked eye	Aqueous solution	[38]
	14.2 nm	0.5 Nm	2-ME/$S_2O_3^{2-}$ -AuNPs	Uv-visspectrometry & naked eye	Aqueous solution (water and soil samples)	[39]
	14.2 ± 0.3 nm	45 nM	2-ME/AuNPs	Uv-visspectrometry & naked eye	Real environmental sample (water and oil)	[22]
	13 nm	500 nM	Unmodified GNPs and DNAzyme	Uv-visspectrometry & naked eye	Environmental samples	[40]
	~47 nm	9 nM	DTT functionalized anisotropic GNPs	Uv-visspectrometry & naked eye	Water	[41]
	13 nm	0.1 μmol/L	CALNN- functionalized GNPs	Uv-visspectrometry & naked eye	Aqueous solution	[42]
	20 nm	0.5 μg/L	Maleic acide functionalized GNPs	Uv-visspectrometry & naked eye	Milk samples	[43]
	13.3 nm	50pM	BSA-AuNPs	Uv-visspectrometry & naked eye	Aqueous solution (water, urine, blood)	[44]
Hg^{2+}	16 ± 1.9 nm	100 nM	DTET-AuNPs	Uv-visspectrometry & naked eye	Aqueous solution	[45]
	13 ± 1 nm	0.1 μM	Tween 20-modified GNPs	Uv-visspectrometry & naked eye	Environmental sample (water)	[30]
	13 ± 1 nm	50 nM	MPA/AMP-capped AuNPs	Uv-visspectrometry & naked eye	High-salt solution	[46]
	13 nm	4×10^{-8} M	ssDNA, dsDNA with GNPs	Uv-visspectrometry & naked eye	Aqueous solution	[47]
	7.9 ± 2.3 nm	40 nM	CEQC-stabilized AuNPs	Uv-visspectrometry & naked eye	Aqueous solution	[48]
	17 ± 2 & 36 ± 2 nm	16 nM	L-Tyrosin-stabilized AuNPs	Uv-visspectrometry & naked eye	Aqueous medium	[37]
	16 nm	100 nM	L-cysteine functionalized GNPs (cys-GNPs)	Uv-visspectrometry & naked eye	Aqueous solution	[29]
Ag^{+}	13 ± 1 nm	0.1 μM	Tween20-modified GNPs	Uv-visspectrometry & naked eye	Environmental samples (water)	[30]
	14.2 ± 03 nm	70 nM	2-ME//AuNPs	Uv-visspectrometry & naked eye	Real environmental sample (water and oil)	[22]
Ca^{2+}	13.5 nm	0.3 μM	Tween20-moodified GNPs	Uv-visspectrometry & naked eye	Serum	[35]
	4.5 nm	–	2-ME/AuNPs	Uv-visspectrometry & naked eye	-	[49]
	–	10 μM	Cysteine/thioglycolate/triethanolamine-modified GNPs	Uv-visspectrometry & naked eye	Water and digested rice samples	[50]
	13 nm	Distinguish between normal and abnormal (hypercalcemia) Ca^{2+} ion level in serum. 2.4 to 3.5 Mm	Calsequestrin-functionalized GNPs	Uv-visspectrometry & naked eye	Blood serum samples	[34]
Cu^{2+}	13 nm	1 nM	Silver-coated GNPs (Ag/AuNPs)	Uv-visspectrometry & naked eye	Aqueous solution	[31]
	13 ± 2 &45 ± 5 nm	2.23 μM	L-cysteine-GNPs	Uv-visspectrometry & naked eye	–	[51]
	13 nm	–	-amyloid peptide (Aβ1-16)-GNPsβ	Uv-visspectrometry & naked eye	Solution and co-culture with SHG-44 cells	[52]
	8.1 ± 1.1 nm	0.04 μM (Uv–vis) 2 μM (naked eye)	Bare GNPs	Uv-visspectrometry & naked eye	Water samples	[53]

(*continued on next page*)

Table 1 (*continued*)

Ions	Size of nanoparticles	Detection of limit (LOD)	Gold nanoparticles	Detection method	Samples	Ref
No^{2-}	~33 nm	1 ppm	MTT-GNPs	Uv-visspectrometry & naked eye	Aqueous solution	[54]
	–	<1 ppm	4-ATP modified GNR	Uv-visspectrometry & naked eye	Drinking water	[32]
Mg^{2+}	4.5 nm	–	ACEADD-GNR	Uv-visspectrometry & naked eye	-	[49]
Zn^{2+}	13 nm	–	-amyloid peptide (Aβ1-16)-GNPsβ	Uv-visspectrometry & naked eye	Solution and co-culture with SHG-44 cells	[52]
S^{2-}	8.1 ± 1.1 nm	80 nM	Bare GNPs	Uv-visspectrometry & naked eye	Water samples	[55]
Ba^{2+}	13 nm	15×10^{-6} M	Tiopronin functionalized GNPs (Tio-GNPs)	Uv-visspectrometry & naked eye	Aqueous solution	[33]
Uo_2^{2+}	13 nm	50 nM	DNAzyme-GNPs	Uv-visspectrometry & naked eye	Water	[36]
Ln^{3+} (Eu^{3+},Sm^{3+})	6.8 ± 1.7 nm	~50 nM	Malonamide-functionalized GNPs	Uv-visspectrometry & naked eye	Aqueous solution	[56]

DTT:dithiothreitol, CALNN: Cys-Ala-Leu-Asn-Asn, DTET: dithioerythritol-modified, MPA/AMP: 3-mercaptopropionate acid (MPA)/adenosine monophosphate (AMP), CEQC: carboxylethylquaternized cellulose, ACEADD: aza-crown ether acridinedione, MTT: 1-(2-mercaptoethyl)-1, 3, 5-triazinane-2, 4, 6-trione.

due to the extraordinary importance of nucleotide sequences in biological analyzes as well as the characteristics and advantages of using gold nanoparticles in detection, such as simplicity, easy preparation, low cost and time saving [24], colorimetric detection method is widely used for detection of DNA. The use of DNA-functionalized MBs (magnet beads) and non-aggregated GNP for detection of oligonucleotide sequences based on colorimetric assay showed that using 30 nm gold nanoparticles in 60 min with a detection limit of 4femtomoles (50 fmol mL^{-}) and using Uv–vis spectroscopy and also color change, oligonucleotide sequences can be detected [24].

It is reported that human p53 gene also detectable using ss-DNA-functionalized gold nanoparticles and based on disassembly/assembly of gold nanoparticles. Also, in this study, by pH changes (with adding HCL) provides optimal conditions with no need to additional DNA probe for detection of DNA of the P53 Gene. In this study, it has been reported that by providing these conditions, the 12-point mutation in the p53 gene is detected [58].

2.2.2.1. Detection of microorganisms. Another application of the colorimetric detection method is detection of bacteria. In this way, using gold nanoparticles, the genetic material of bacteria (including dsDND and ssDNA) detected and the result can be examined and analyzed by Uv–vis spectroscopy and observing the change in the color of the solution with the naked eye. Among the bacteria that can be detected in this way, include; *Bacillus anthracis* bacterium with detection of ssDNA and dsDNA resulting from asymmetric polymerase chain reaction)AS-PCR([21] and detection of DNA of *Listeria monocytogenes* after the PCR, this bacterium causes food contamination and creating Listeriosis and has symptoms similar to central nervous system damage [59]. In addition, detection of (149 bp) dsDNA of E.coli by using DNA-functionalized GNPs [60], detection of 18 s RNA of Leishmania pathogens [61] and also DNA of Salmonella after performing PCR technique [62]. These bacteria cause disease, disability and mortality in human thus rapid and accurate detection of these microorganisms is very important.

2.2.3. Detection of protein, enzyme and amino acid

Many attempts have made recently in making nanoparticles and methods for the application of these particles staking into account their specific properties, for detection of biological targets. With advancement of the sensitivity and selectivity of the colormetic method, it can be used for detection of proteins including markers of diseases and pathogens. So we can examine the results only by observing color change in solution of the nanoparticle with the naked eye and complicated instrument is not necessary [63].

In Table 2, in different studies a number of proteins, amino acids and enzymes have described. Among them: the lysozyme enzyme that has been reported detectable using gold nanoparticles of 13 nm conjugate with human albumin serum (HAS) based on aggregation of gold nanoparticles with a minimum detection limit of 50 nM and HSA is an effective factor in stabilizing gold nanoparticles in high salt concentrations, and also with interaction with lysozyme and causes detection of this analyte. This method is an appropriate method for detecting and analyzing lysozyme in egg whites [64]. In addition, the telomerase, which is one of the cancer biomarkers, detected by this method. This rapid and high sensitive method has been used in detection of this enzyme. So that in presence of telomerase, the nucleic acid bounding to the surface of the nanoparticle is not digested by Exonuclease I and the gold nanoparticle solution remains aggregated, but in the absence of telomerase, Exonuclease I causes digestion of nucleic acid binding and results in the dispersion of aggregated nanoparticles [65].

Jia-Lin Hui et al. reported a study using Colorimetric detection on inhibitory and activity of the enzyme SAHH(S-Adenosylhomocysteine Hydrolase). The SAHH enzyme causes hydrolysis of SAH to homocysteine and adenosine. SAHH inhibition used in parasitic diseases; on

Table 2
Amino acids, proteins and enzymes detected by the colorimetric detection method and details of these analytes.

Analyte	Size of nanoparticles	Detection of limit (LOD)	Gold nanoparticles	Detection method	Ref
Lysozyme	13 nm	50 Nm	Albumin-modified GNPs	Uv-visspectrometry & naked eye	[64]
	15 nm	16 Nm	Aptamer-conjugated GNPs	Uv-visspectrometry & naked eye	[63]
Dopamine	–	0.07 μM	AHMP-functionalized GNPs	Uv-visspectrometry & naked eye	[74]
	–	2×10^{-7} M	GNPs and Cu^{2+} ions	Uv-visspectrometry & naked eye	[75]
Cysteine	20 nm	100 Nm	Oligonucleotid-functionalized AuNPs	Uv-visspectrometry & naked eye	[76]
	–	1 μM (naked eye) 10 nM (Uv photometry)	Unmodified AuNPs	Uv-visspectrometry & naked eye	[77]
SOD1	19 ± 3 nm	–	SOD1 monomers-functionalized GNPs	Uv-visspectrometry & naked eye	[67]
	20 nm	–	SOD1 conjugated GNPs	Uv-visspectrometry & naked eye	[68]
PDGF	13 nm	0.25 nM	Aptamer-GNPs	Uv-visspectrometry & naked eye	[78]
	13 nm	nM level	Aptamer-GNPs	Uv-visspectrometry & naked eye	[79]
Flt-1	13 ± 2 nm	0.2 nM	Peptide-coated GNPs	Uv-visspectrometry & naked eye	[80]
Telomerase	12 nm	29HL-60 cells mL^{-1}	Telomerase primer (TP)-modified GNPs	Uv-visspectrometry & naked eye	[65]
Glutathione	13 ± 1.7 nm	2.9×10^{-8} mol/L	Water-soluble copolymers attached to GNPs	Uv-visspectrometry & naked eye	[81]

AHMP: 4-amino-3-hydrazino-5-mercapto-1,2,4-triazol, SOD1: superoxide dismutase.

the other hand, the activity of this enzyme in immunodeficiency disease and genetic disorder is also discussed. Sensitive but costly and time-consuming methods such as high performance liquid chromatography with fluorescence and capillary electrophoresis with UV absorption are available to examine the performance of this enzyme. However, in this study, because fluorosurfactant-capped AuNPs (FSN-AuNPs) is susceptible to homocysteine and cysteine, if SAHH affects SAH and cause its hydrolysis to adenosine and homocysteine, nanoparticles are aggregated and solution color is changed. But if with inhibiting the activity of SAHH by adenosine and thereby inhibiting SAH hydrolysis to adenosine and homocysteine, aggregation of nanoparticles does not occur due to absence of homocysteine and thus activity and inhibition of the enzyme SAHH could be investigated [66].

Function of other enzymes has also been studied with this method using conjugated gold nanoparticles with different functional groups in various studies. SOD1 enzyme with gold nanoparticles conjugated with SOD1 monomers [67,68], kinases protein based on non-cross-linking [25], and also based on phosphorylation and aggregation of gold nanoparticles in an interaction with a phosphorylated substrate [69], like protein kinase Cα, in detecting breast cancer based on peptide substrate phosphorylation with pk Cα, which prevents the aggression of gold nanoparticles. However, in absence of peptide substrate phosphorylation, aggregation of nanoparticles is not observed and change in the color of the solution is observed. The results of this study indicate that color changes are observed in 12 samples of 18 Breast cancer samples [70]. Examination of Heterogeneous-catalyzed Lipase activity with Tween20-GNPs with detection of limit (LOD) 2.8×10^{-2} mg/mL [71], study of Pyrophosphatase (PPase) activity with gold nanoparticles cysteine-stabilized [72], as well as inhibition and activity of endonuclease/methyl transferase using DNA-assembly AuNPs [73].

2.2.4. Detection of other analytes

Melamine (1,3,5-triazine-2,4,6-triamine, $C_3H_6N_6$) is an organic compound which is used in plastic industry, fertilizers, and resin. Due to it has high nitrogen content (66% by mass) has been also used as an additive adulterant food and is widely added to, infant formula milk and pet food. Its high concentration is harmful and toxic, so detection of melamine with high-sensitivity is very important [82,83]. In the following, three different studies that have examined this organic composition based on colorimetric detection method are reviewed. Detection of melamine based on attachment of amine melamine groups and $AucL_2^-$/$AucL_4^-$ on gold nanoparticles surface cause organic detection with 2×10^{-7} gL^{-1} [84]. Chitosan-stabilized AuNPs is shifted in presence of surface Plasmon bond melamine and cause solution color change from red to dark blue and detection of melamine with detect limit of 6×10^{-6} g/L (Uv–vis) is reported [83]. Also, detection of this organic compound with thymine derivative (NT) decorated AuNPs, based on the binding of thymine and melamine resulted in a change in the color of the solution, resulting in observing change in the color with naked eye, at a detection limit of 5.3 nM in the milk [82].

It is reported that cervical carcinoma cells (Hela cells) can also be detected by this method. The folic acid receptor is expressed in large numbers in Hela cells. By binding the folic acid conjugated to gold nanoparticles (FA-GSH-GNPs) to its receptor on Hela cancer cells, in this study, these cells are detected with a threshold of 10^2 cells/mL [85]. Also, the direct detection of the cancer cells; CCRF-CEM cells (CCL-119 T-cell, human acute lymphoblastic leukemia) and Ramos cells (CRL-1596, B-cell, human Burkitt's lymphoma) with gold nanoparticles conjugated to aptamer (ACGNPs: aptamer-conjugated gold nanoparticles) that due to unique spectral properties of gold nanoparticles and selectivity and high specificity of aptamer, causes detection with high sensitivity and selectivity [86].

H_2S is water-soluble, flammable and toxic gas that is considered as environmental pollutant component. Abnormality on surface of H_2S is also associated with diseases like Alzheimer's disease and Down syndrome. Detection of this gas with gold nanoparticles (13 nm) Thiolateazido derivatives and active esters functionalized gold nanoparticles (AE–AuNPs) based on the aggregation of gold nanoparticles in the presence of H_2S gas with detect limit 0.2 μM, with Uv–vis and 4 μM with naked eye is performed [87].

2.3. Colorimetric immunoassay

As noted above, various functional groups are conjugated to gold nanoparticles and used in analytes analyzers. One of cased conjugated to gold nanoparticles and used in detection is special antitumor antibody, that is detection of target analytes is performed based on immunoassay.

Immunoassay based on gold nanoparticles is dramatically have been used in various areas like analytes detection [88]. Examining Human Pancreatic Carcinoma tissue conjugated with gold nanoparticles anti-F19 monoclonal anti-tumor antibodies and observing with dark field microscopy at maximum resonance scattering [89]. Detection of DDT (1,1,1-trichloro-2,2-bis (4-chlorophenyl)ethane) pesticide in environment and food samples)Given that this gold nanoparticles replace the enzyme to label with antibodies in detection of pesticides and is much more stable than other fluorescent colors and enzymes, and is suitable for pesticide immunoassay([88]. Direct detection of atrazin pesticide and examination of signal in atrazin special antibody with pesticide by differential pulse voltammetry (DPV) [90].

Based on functional groups of GNP, various colorimetric assays have been developed for detection of analyte such as proteins, nucleic acid and cell. The conjugated antibody to the GNP is one of the functional groups used in detection of analyte with high sensitivity and specificity and cause expansion of colorimetric immunoassay method [91]. Solution color change from red to blue/purple and vice versa, based on the

aggregate state and disperse of nanoparticles, as well as high specificity and sensitivity are significant advantages of this method, which can be widely used in detection.

Among the studies performed based on a colorimetric immunoassay, our study is on the use of this method for the detection of prostate-specific antigen using gold nanoparticles (25 nm) conjugated with specific antibody PSA based on the colorimetry system. Thus, based on the aggregation GNPs in interaction of the conjugated nanoparticles with target, and finally, observation of solution color change with the naked eye and Uv–vis spectrophotometer, detection of PSA antigen in concentrations greater than 5 ng/mL is possible. Compared with other methods, is an appropriate and new method for detection of prostate cancer in the early stages of the disease [92].

Other studies conducted on detection of analyte based on a colorimetric immunoassay include; Detection of neurogenic 3 (ngn 3) that is pancreatic endocrine precursor [93]. Detection of diabetic biomarker marker glycated hemoglobin (HbA1c) [94], detection of aflatoxin B1 using magnetic beads (MBs) and gold nanoparticles labeled with anti-A antibodies AFB [95], detection of IgG using a 15-nm protein-modified gold nanoparticle based on transfer radical polymerization (ATRP) technology in range 0.5–25 ng/mL with minimum detection 0.03 ng/mL [91]. And also, detection of Abseisic Acid Glucose Ester (ABA) that is a herbal with conjugated nanoparticles to CALNN (Cys-Ala-Leu-Asn-Asn) [96] and detection of alkaline phosphatase (ALP) and Avian Influenza virus particles with high sensitivity [97].

Na Li et al. provided a critical coagulation concentration (CCC)-based salt titration method in detection of analyte as visual, as well as enhancement of colorimetry quality with gold nanoparticles in order to change the color from red to blue rapidly (in the presence of analyte) in form of a study [98]. In addition, sensitivity of GNPs in colorimetric detection can be improved by reducing electrostatic repulsion. In this regard, a study has been performed, and the provided model thioctic acid-stabilized GNPs has been used in it and it is stated that this guideline reduces the limit of detection (LOD) [99].

3. Conclusions

In recent years, the use of nanoparticles, especially gold nanoparticles (GNPs) in various fields of medicine including drug delivery, vaccine development and biosensorics, has expanded due to having unique chemical and physical characteristics such as optical properties, simple use and compatibility. One of the most important applications of this particles is detection of is the various materials. Quick and accurate detection of material in various fields, including medicine and environmental monitoring is of great importance.

Colorimetry is a solution-based method; that due to unique properties of gold nanoparticles these particles are used in the materials detection and colorimetric detection using these particles due to the color change characteristic following mode shift (aggregation and non-aggregation) these particles are examined in detection of different analytes. According to aggregated and non-aggregated modes of the gold nanoparticles, color change in from red to blue/purple and vice versa is observed. In fact, in the presence of target analytes, the aggregate and non-aggregate modes of nanoparticles (Bare gold nanoparticles or functionalized with different compositions) change and eventually observed as a change in solution color.

The aggregation of nanoparticles occurs in the presence of target analytesis mainly due to functionalized groups that bind to nanoparticles. One of these functional groups is a special anti-target antibody, which is basis of the method of colorimetric immunoassay in materials detection attaches to gold nanoparticles and due to its high affinity and high specificity; it can be used in detection of materials with high accuracy and precision.

Analytes, which have been investigated and detected by the method of colorimetric detection, mainly consist of cells, DNA, proteins, small molecules and ions, including metal ions. The advantages of this method is detection of analyte with naked eye, and no need for advanced and expensive equipment, only based on the observation of the solution color change in the presence or absence of target analyte. In addition, high speed and simplicity of method, saving in cost, time, and detection of materials with a low detection of limit (LOD) cause this method to be superior compared to other detection methods.

Disclosures

The authors have no conflicts of interest to declare.

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